

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Jan Wadstein *et al.*

Serial No.: 09/410,484

Group No.: 1616

Filed: September 30, 1999

Examiner: Arnold, Ernst

Entitled: **METHOD OF TREATING HYPERTENSION AND REDUCING  
SERUM LIPASE ACTIVITY**

**APPELLANTS' REPLY BRIEF**

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Appeal Brief - Patents  
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Dated: March 23, 2009

By: /Michele R. Gilmer/  
Michele R. Gilmer

Dear Examiner Ernst:

This Reply Brief is in reply to the Examiner's answer mailed January 23, 2009.

Appellants hereby authorize the Commissioner of the Patent and Trademark Office to charge the fees required under § 41.20(b)(2), any required fee for any Petition for Extension of Time, and any other fee for filing this Brief to Attorney Deposit Account No. 50-4302. Please reference Attorney Docket No.: NATNUT-03972 when charging the Attorney Deposit Account.

**STATUS OF THE CLAIMS**

1. (Previously presented) A method of treating hypertension in humans comprising:
  - a) providing a hypertensive human patient in need of hypertension treatment and a composition comprising a safe and effective amount conjugated linoleic acid for treating hypertension; and
  - b) administering said conjugated linoleic acid composition to said human patient so that blood pressure of said human patient is reduced.
2. (Previously presented) The method of Claim 1 wherein the conjugated linoleic acid composition is a mixture of octadecadienoic acid isomers selected from the group of cis-9, trans-11; cis-9, cis-11; trans-9, cis-11; trans-9, trans-11; cis-10, cis-12; cis-10, trans-12; trans-10, cis-12; trans-10, trans-12 octadecadienoic acid.
3. (Previously presented) The method of Claim 1 wherein the conjugated linoleic acid composition consists essentially of octadecadienoic acid isomers selected from 9,11 octadecadienoic acid, 10,12 octadecadienoic acid, and mixtures thereof.
- 4-6. (Cancelled).
7. (Previously presented) The method of Claim 1 wherein the conjugated linoleic acid is administered orally.
8. (Withdrawn) The method of Claim 1, wherein the conjugated linoleic acid is provided in a prepared food product.
9. (Previously presented) The method of Claim 1 wherein said safe and effective amount of conjugated linoleic acid is about 0.1 grams to 20 grams.
10. (Withdrawn) A method of reducing serum lipase activity in humans comprising
  - a) providing a subject and a composition comprising a safe and effective amount conjugated linoleic acid; and
  - b) administering said conjugated linoleic acid composition to said subject under conditions such that serum lipase activity of said subjects is reduced.

11. (Withdrawn) The method of Claim 10 wherein the conjugated linoleic acid composition is a mixture of octadecadienoic acid isomers selected from the group of cis-9, trans-11; cis-9, cis-11; trans-9, cis-11; trans-9, trans-11; cis-10, cis-12; cis-10, trans-12; trans-10, cis-12; trans-10, trans-12 octadecadienoic acid.

12. (Withdrawn) The method of Claim 10 wherein the conjugated linoleic acid composition consists essentially of octadecadienoic acid isomers selected from 9,11 octadecadienoic acid, 10,12 octadecadienoic acid, and mixtures thereof.

13. (Withdrawn) The method of Claim 10 wherein said conjugated linoleic acid composition comprises esters of conjugated linoleic acid.

14. (Withdrawn) The method of Claim 13 wherein said esters are selected from methyl esters and ethyl esters.

15. (Withdrawn) The method of Claim 10 wherein said conjugated linoleic acid composition comprises triglycerides including at least one conjugated linoleic acid at the SN-1, SN-2, or SN-3 position of said triglycerides.

16. (Withdrawn) The method of Claim 10 wherein the conjugated linoleic acid is administered orally.

17. (Withdrawn) The method of Claim 10 wherein the conjugated linoleic acid is provided in a prepared food product.

18. (Withdrawn) The method of Claim 10 wherein said safe and effective amount of conjugated linoleic acid is about 0.1 to 20 grams.

**GROUND OF REJECTION TO BE REVIEWED ON APPEAL**

There is one grounds of rejection to be reviewed on appeal:

Whether Claims 1-3, 7 and 9 are obvious over Cook et al. (U.S. Pat. No. 5,554,646) in view of Kawamura et al. (Hypertension 1996, 27, 408-413) and Shinitzky (U.S. Pat. No. 4,474,773).

## **ARGUMENT**

The Office's acceptance of the statements of the real party in interest, related appeals and interferences, status of claims, status of amendments after final, summary of invention, grounds of rejection, and claims appealed is appreciated. Appellants reiterate their previous arguments that the Office has made scientifically incorrect and unsupportable assumptions about the teachings of Cook and Shinitzky and has failed to consider pertinent rebuttal evidence established in the Declarations of Mr. Asgeir Saebo and Dr. Inge Bruheim. As a result, the Office has either has not established a *prima facie* case of obviousness, or, in the alternative, any *prima facie* case of obviousness established has been properly rebutted by Appellants. Accordingly, Appellants request that the current rejections of the claims be withdrawn. Below, Appellants respond to the arguments presented by the Examiner in the Examiner's Answer.

### **1. Summary of the Examiner's rejection**

The rejection by the Examiner is based on three references, Cook et al. (U.S. Pat. No. 5,554,646); Kawamura et al. (Hypertension 1996, 27, 408-413) and Shinitzky et al. (U.S. Pat. No. 4,474,773). The Examiner states that Cook et al. disclose a method of reducing body fat comprising the administration of conjugated linoleic acid. Examiner's Answer at 4. The Examiner states that Kawamura et al. 1) provides a nexus teaching between hypertension, weight loss and decreases in blood pressure, and 2) teaches that changes in body weight exhibited significant correlations with blood pressure reduction in hypertensive overweight human patients. *Id.* The Examiner states that Shinitzky et al. teach methods of treating warm-blooded animals comprising administering a pharmaceutically effective amount of a composition comprising 5-10% linoleic acid for the treatment of hypertension, citing claims 1, 4, and 24. *Id.* The Examiner then states that it would have been obvious to one of skill in the art at the time the claimed invention was made to treat a hypertensive patient with the conjugated linoleic acid method of Cook et al. and produce the instant invention. *Id.* at 5. The Examiner admits that Cook et al. does not teach a method of treating hypertension in humans. *Id.*

The Examiner supports the rejection with the following arguments:

- One or ordinary skill in the art would have been motivated to produce the invention because Cook et al. provide a method of reducing body fat and Kawamura et al. teach that a reduction in weight in hypertensive patients results in a lowering of blood pressure. *Id.* at 5.
- Shinitzky et al. provide the teaching that linoleic acid can be used to treat hypertension. *Id.* at 5.

- Since conjugated linoleic acid is a mixture of positional and geometric isomers of linoleic acid, then one of ordinary skill in the art would immediately envision conjugated linoleic acid in the treatment of hypertension. *Id.* at 5.
- Evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. *Id.*

Below, Appellants explain why the majority of these alleged facts, assumptions, and conclusions are either incomplete or scientifically correct and why a person of ordinary skill in the art would not reach the same conclusions as the Examiner. Appellants also discuss the failure of the Examiner to respond to factual evidence introduced into the record by Appellants.

**2. Cook et al. does not teach that conjugated linoleic acid reduces bodyweight**

The Examiner states that Cook *et al.* disclose a method of reducing body fat comprising the administration of conjugated linoleic acid. Examiner's Answer at 4. This statement is correct. However, Cook *et al.* does not teach that administration of conjugated linoleic acid reduces bodyweight. In fact, Example 4 of Cook *et al.* explicitly teaches that when mice are fed a test diet containing conjugated linoleic acid or a control diet containing corn oil (which contains regular c9, c12 linoleic acid as established in the Bruheim Declaration, paragraph 3), the mice fed conjugated linoleic acid have reduced body fat as compared to the controls, but the bodyweight is the same. Cook *et al.*, Column 3, lines 28-33. In Example 3, Cook *et al.* state that CLA administration reduces body fat in humans, but is silent as to whether bodyweight is decreased.

This is a key distinction because the Examiner makes an attempt to link the teachings of Cook et al. and Kawamura et al. by arguing that Kawamura et al. is a nexus teaching between hypertension, weight loss and decreases in blood pressure and that "One of ordinary skill in the art would have been motivated to produce the invention because Cook Appellants. provide a method of reducing body fat and Kawamura et al. teach that a reduction in weight in hypertensive patients results in a lowering of blood pressure." Examiner's Answer at 5. The Examiner's confusion of the facts is demonstrated at page 12 of the Examiner's Answer where the Examiner states:

- Conjugated linoleic acid is taught to reduce body weight;
- bodyweight reduction is correlated with decrease in blood pressure in overweight hypertensive patients;
- linoleic acid is used to treat hypertension; and

- there is no teaching at the time of the invention which would suggest to one of ordinary skill in the art that conjugated linoleic acid would increase blood pressure.

Examiner's Answer at 12. In the Examiner's first bullet point, the Examiner has switched the finding that Cook et al. teaches the use of conjugated linoleic acid to reduce body fat (*see, e.g.*, Examiner's Answer at 4) to the finding that "conjugated linoleic acid is taught to reduce body weight." Cook et al. does not teach this. Cook et al. teaches that body fat is reduced. As shown in the Examples of Cook et al., this does not mean that bodyweight is reduced. This is exactly what Example 4 of Cook et al. teaches one of skill in the art. This is why, as Appellants argued in their Appeal Brief, that the Examiner's arguments are not scientifically valid and that the Examiner's assumptions regarding the prior art are incorrect.

In response to these arguments, the Examiner refers to the bullet pointed facts presented in the Applicant's Appeal brief and states that "None of these assertions address the fact that overweight patients can be hypertensive and lowering the body weight reduces blood pressure as taught by Kawamura et al. The Examiner cannot simply ignore the teachings in the art. Kawamura et al. clearly teach a patient population where weight loss positively correlated with reduced blood pressure in hypertensive patients. **The method of Cook et al. is broad and includes reducing the body fat in overweight hypertensive patients in need of hypertensive treatment.** The instant claims are not distinguished from that population." Examiner's Answer at 10-11, (emphasis Examiner's). This reasoning is flawed. Cook et al. does not teach that conjugated linoleic acid reduces bodyweight, thus the Examiner's attempt to link administration of conjugated linoleic acid to a decrease in bodyweight and thus reduced blood pressure is not supported by the references. The Examiner has assumed that Cook et al. teaches a reduction in bodyweight. This assumption is not supported by Cook et al. The bolded language of the Examiner is also not supported by Cook et al. Cook et al. makes absolutely no mention of hypertensive patients and does not indicate that human males referred to in Example 3 suffered from hypertension.

Finally, Appellants further note that Shinitzky et al. does not cure these defects in the Examiner's argument. In fact, Example 5 of Shinitzky et al. teaches that rats fed either the complex lipid mixture or a control showed no difference in weight. Shinitzky et al., Column 12, lines 13-14.

### **3. The Examiner has overstated the teaching of Shinitzky**

The Examiner states that "Shinitzky et al. provide the teaching that linoleic acid (C18:2, cis-9, cis-12) can be used to treat hypertension." Examiner's Answer at 5. At best, Shinitzky

teaches that a complex lipid mixture can be used to treat hypertension. As Appellants previously argued in their Appeal Brief, claims 1, 4, and 24 teach that hypertension can be treated by administering a complex mixture comprising “a lipid fraction derived from natural sources (AL), said lipid fraction containing 40-80 weight percent glycerides, 3-5 weight percent cholesterol, 10-30 weight percent lecithin (phosphatidyl choline), 5-15 weight percent phosphatidyl ethanolamine and 2-5 weight percent negatively charged phospholipids, wherein the ratio of unsaturated to saturated fatty acids is at least 1:1” (Claim 1) and that the fatty acid component of this complex mixture comprises “Palmitic acid 35-45%, oleic acid 35-45%, linoleic acid 5-10%, stearic acid 5-7%, palmitoleic acid 2-3%, arachidonic acid 0.2-1%” (Claim 4). *See Shinitzky et al.*, Claims 1 and 4 and Bruheim Decl. at ¶2. The Bruheim Declaration directly addresses this issue. As established by Dr. Bruheim:

- *Shinitzky et al.* does not teach that linoleic acid can be used to treat hypertension or that among all of the components of the complex mixture, linoleic acid is sufficient to treat hypertension.
- *Shinitzky et al.* teaches that a complex lipid fraction can be used to treat hypertension.
- This is not the same as teaching that linoleic acid can be used to treat hypertension.
- One of skill in the art would recognize that any of the other components could be responsible for the hypertensive effect or that a combination of the components is necessary.

Bruheim Decl. ¶2 (p. 20 in Section IX of Applicant’s Appeal Brief).

As can be plainly seen, the invention claimed in claims 1, 4, and 24 utilizes a complex lipid mixture, of which linoleic acid is only a small part. Thus, it is an overstatement to state that *Shinitzky* teaches that linoleic acid can be used to treat hypertension.

In response to these arguments, the Examiner states:

It is clear and concise that *Shinitzky et al.* disclose a method of treating hypertension using a composition comprising linoleic acid. The claim language of *Shinitzky et al.* is not ambiguous or vague or unclear. It is unthinkable to come to any other conclusion. This has been known in the art since 1984.

Examiner’s Answer at 7. Again, the Examiner’s arguments are inconsistent. Stating that *Shinitzky et al.* teaches that linoleic acid can be used to treat hypertension (*See, e.g.,* Examiner’s Answer at 5) is different from arguing that *Shinitzky et al.* teaches a composition comprising linoleic acid is used to treat hypertension. Thus, in making the rejection, the Examiner relied on a different fact (*Shinitzky et al.* teaches the use of linoleic acid to treat hypertension) than is



relied on in responding to Applicant's arguments. Examination of the Examiner's bullet points on page 12 of the Examiner's Answer makes this point crystal clear. The Examiner states that he has shown at the time of the invention "linoleic acid is used to treat hypertension." This is an overstatement.

This response by the Examiner completely ignores bullet-pointed facts listed above that were established in the Bruheim Declaration. Appellants respectfully submit that a person of skill in the art, upon consideration of Shinitzky *et al.*, would not conclude that Shinitzky *et al.* teaches that linoleic acid, in isolation, can be used to treat hypertension. The Bruheim Declaration is unequivocal on this fact and discusses the complex nature of the composition taught in Shinitzky *et al.* Instead of responding to these facts and engaging in a discussion on what Shinitzky actually teaches (*i.e.*, the use of a complex lipid mixture), the Examiner makes an argument based on the use of the term "comprising" in the claims of Shinitzky by stating that the Shinitzky *et al.* teaches the use of a composition comprising linoleic acid. However, the argument ignores the complex nature of the composition used in Shinitzky *et al.* It is telling that the Examiner never rebuts or addresses the fact that the linoleic acid is only a small component of the complex mixture claimed in Shinitzky *et al.* The Examiner is clearly trying to ignore or dismiss facts that do not support his arguments. When a patent applicant puts forth rebuttal evidence, the Office must consider that evidence. *Id.*, see also *In re Soni*, 54 F.3d 746, 750 (Fed.Cir.1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability). It is error not to consider and properly address this evidence.

**4. The Examiner has ignored evidence presented by Appellants that conjugated linoleic acid has different properties than regular linoleic acid**

Even if the Examiner was correct that Shinitzky *et al.* teaches that linoleic acid can be used to treat hypertension, the Examiner has ignored the evidence presented by Appellants that linoleic acid and conjugated linoleic acid have different properties and thus it is unpredictable that conjugated linoleic acid could be used to treat hypertension. Appellants first respectfully note that conjugated linoleic acid is a separate and distinct composition from linoleic acid. Conjugated linoleic acid is defined in the specification as:

any conjugated linoleic acid or octadecadienoic free fatty acid. It is intended that this term encompass and indicate all positional and geometric isomers of linoleic acid with two conjugated carbon-carbon double bonds any place in the molecule. CLA differs from ordinary linoleic acid in that ordinary linoleic acid has double bonds at carbon atoms 9 and 12. Examples of CLA include cis- and trans isomers ("E/Z isomers") of the

following positional isomers: 2,4-octadecadienoic acid, 4,6-octadecadienoic acid, 6,8 - octadecadienoic acid, 7,9 - octadecadienoic acid, 8,10- octadecadienoic acid, 9,11- octadecadienoic acid and 10,12 octadecadienoic acid, 11, 13 octadecadienoic acid.

Specification, p. 5, l. 25 – p. 6 l. 5. Thus, linoleic acid and conjugated linoleic acid are different compositions. This is confirmed by the Examiner at page 8 of the Examiner's Answer. Linoleic acid has double bonds at the 9 and 12 positions of the linoleic acid molecule, while conjugated linoleic acid has conjugated double bonds, i.e., the double bonds are only two positions apart as opposed to three positions apart.

The Examiner relies on case law to establish the proposition that similar properties may normally be presumed when compounds are very close in structure and that “evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious.” *Citing In re Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. In response to this argument, Appellants have presented the Bruheim Declaration. The Bruheim Declaration established that:

- Conjugated isomers of conjugated linoleic acid have different biological properties than linoleic acid.
- This was known in the art prior to the filing date of this application and has been substantiated in many publications after the filing date of this application.
- The references attached to the Bruheim Declaration establish that the conjugated isomers of linoleic acid have distinct biological properties as compared to standard linoleic c9,c12 linoleic acid.
- Many of these references utilize corn oil, which comprises c9,c12 linoleic acid, as a control.
- All of the references show that the conjugated linoleic acid isomers have distinct biological properties.
- Dr. Mark Cook, the inventor of the cited 5,554,646 patent, is an author on most of these publications.

Bruheim Declaration ¶3 (p. 21 in Section IX of Appeal Brief).

In response to this evidence, the Examiner argues that “a critical comparison of the biological properties of between linoleic acid and the mixture of isomers that comprises conjugated linoleic acid would have taken into consideration which isomers are present and in what ratios. Failing that, it is reasonable to assert that the isomers have similar properties. In

fact similar properties may normally be presumed when compounds are very close in structure . . .”

Appellants respectfully submit that this is not a valid distinction and does not address the facts or the references cited in the Saebo Declaration. In effect, the Examiner has failed to address the facts established by Dr. Bruheim and the very clear teaching of the references cited by Dr. Bruheim. The claims are directed to a use of conjugated linoleic acid. The Examiner has asserted that linoleic acid could be expected to have the same properties as conjugated linoleic acid. The difference in properties of conjugated linoleic acid as opposed to linoleic acid is exactly what is addressed by Dr. Bruheim and correlates exactly to the broad assumptions made by the Examiner regarding differences between conjugated linoleic acid and linoleic acid. Appellants respectfully note that the Dr. Bruheim does not make unsupported conclusory statements – he has cited to and provided the references that show that conjugated linoleic acid has different properties than linoleic acid. Appellants respectfully submit that instead of addressing this evidence, the Examiner has constructed a straw-man of a “critical comparison of mixtures of isomers.”

Appellants respectfully direct the Office’s attention to the references provided by Dr. Bruheim. In many of these references, the effect of conjugated linoleic acid was compared to controls, fed either corn oil or linoleic acid. The researchers in these peer-reviewed publications apparently saw no need to compare mixtures of isomers to provide a “critical comparison.” Instead, conjugated linoleic acid was compared to a control. For the Office’s convenience, example test diets and controls from these papers are listed here, with citation to the publication and page of the Appeal Brief where the publications are provided:

- Mice were fed either a basal diet comprising 2.5% linoleic acid or the basal diet containing either 0.5% added Menhaden fish oil or 0.5% added conjugated linoleic acid. Miller CC, Park Y, Pariza MW, Cook ME. Feeding conjugated linoleic acid to animals partially overcomes catabolic responses due to endotoxin injection. *Biochem Biophys Res Commun.* 1994 Feb 15;198(3):1107-12 at 1108; Appeal Brief at 24.
- After a 5-d adaption period mice were randomly separated into groups and fed either control diet (5.5% corn oil) or CLA-containing diet (5.0% corn oil plus 0.5% CLA). Park Y, Albright KJ, Liu W, Storkson JM, Cook ME, Pariza MW. Effect of conjugated linoleic acid on body composition in mice. *Lipids.* 1997 Aug;32(8):853-8 at 853-54; Appeal Brief at 59-60.
- The animals were fed a control diet containing corn oil or a test diet containing corn oil supplemented with conjugated linoleic acid. Chin SF, Storkson JM, Albright KJ, Cook ME, Pariza MW. Conjugated linoleic acid is a growth factor for rats as shown by enhanced weight gain and improved feed efficiency. *J Nutr.* 1994 Dec;124(12):2344-9 at 2345; Appeal Brief at 66.

In sum, Appellants submit that the Declaration of Dr. Bruheim should be given weight and considered. The Examiner cannot simply dismiss the evidence in the Declaration by arguing that a critical comparison requires consideration of isomer mixtures. The Declaration is consistent with the scope of the claims, which are directed to the use of conjugated linoleic acid, and with the scope of the cited prior art, which utilized c9,c12 linoleic acid, such as is found in corn oil as established by Dr. Bruheim.

Appellants respectfully submit that, as above, the Examiner is trying to ignore or dismiss facts that do not support his arguments. When a patent applicant puts forth rebuttal evidence, the Office must consider that evidence. *Id.*, see also *In re Soni*, 54 F.3d 746, 750 (Fed.Cir.1995) (stating that “all evidence of nonobviousness must be considered when assessing patentability”). It is error not to consider and properly address this evidence. Appellants respectfully submit that this evidence establishes that one of skill in the art would clearly recognize that conjugated linoleic acid has different properties than linoleic acid. Thus, Appellants have rebutted the Examiner’s proposition that evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious.

**5. Appellants have established that there is no nexus between weight loss and reduction of hypertension when an active agent is utilized**

As discussed above, there is no evidence that conjugated linoleic acid causes weight loss. However, Appellants also have established through the Declaration of Mr. Saebo that when an active ingredient is given to a subject that causes weight loss, there is no expectation that hypertension will be reduced just because weight loss occurs. Therefore, even if the Examiner were correct that conjugated linoleic acid causes weight loss, it is not correct to make the conclusion that because weight loss occurs, hypertension will be reduced.

In response to this argument, the Examiner asserts that:

Appellant attempts an argument that active agents that cause weight loss can also cause hypertension and that the active agent can have other effects unrelated to weight loss. This is true for some actives such as ephedrine.

Examiner’s Answer, p. 11. This is the point Appellants submitted the evidence to make. Kawamura did not utilize a biologically active agent. This evidence submitted by Appellants rebuts the Examiner’s assertion that there is some nexus between reduction and body weight and decreased blood pressure when a biologically active agent is evolved in the equation. This is what was established in the Saebo Declaration.

The Examiner's further argues that Appellant's arguments are flawed because the evidence submitted regarding the elevation of F2-isoprostanes by conjugated linoleic acid was not available at the time of the invention. Examiner's Answer at 11. This is true, however, the data is relevant to the issue of the fact that when biologically active agent such as conjugated linoleic acid is administered to a subject that there can be a variety of effects, which is the issue addressed by the Saebo Declaration. See Saebo Declaration, Appellant's Brief at p. 78. Elevation of F2-isoprostanes is one of those effects, and it is inconsistent with reduction of blood pressure.

The Examiner then argues that "without hard facts concerning the action of CLA in the body, such as an assertion that administration of CLA would result in an increase in blood pressure is merely speculation without proof. The hard fact is that there is nothing in the art at the time of the invention that would suggest conjugated linoleic acid elevates blood pressure." Examiner's Answer at 12. Appellant's respectfully submit that this reasoning by the Examiner can just as easily be applied to the Examiner's arguments regarding the nexus between weight reduction, decreased blood pressure, and administration of linoleic acid. The Examiner's assertion that there is such a nexus is merely speculation.

In any event, Appellants respectfully submit that the Examiner has again failed to address or rebut the evidence submitted in the Saebo Declaration. The Saebo Declaration was submitted to establish the fact that when an active agent is biologically active agent, such as CLA, is administered to a subject there can be a variety of unpredictable effects. The Office's primary reasoning supporting its alleged *prima facie* case of obviousness is that Kawamura *et al.* provides a nexus teaching between hypertension, weight loss and decreases in blood pressure. However, Kawamura did not utilize a biologically active agent. However, according to the Office's reasoning, any agent that reduces body weight would also decrease hypertension. The Saebo Declaration directly rebuts the Office's incorrect reasoning.

**6. The Examiner's Answer cites art published well after the priority date of the instant claims**

At page 9 of the Examiner's Answer, the Examiner relies on Alonso et al., J. Dairy Sci. 2003, 86, 1941-46 to respond to Appellants previous arguments that microorganisms that convert linoleic acid into conjugated linoleic acid are not present in humans. Appellants note that this reference was published in 2003, well after the 1999 priority date of the instant application. The reference also suffers from other defects. First, the reference examines the action of *Lactobacillus acidophilus in vitro*. There is no indication that *Lactobacillus acidophilus*

produces CLA *in vivo*. Second, the claims require that conjugated linoleic acid is administered to a subject. Thus, the subject is supplemented with conjugated linoleic acid, the claims do not contemplate administration of linoleic acid followed by conversion. Third, the studies cited above, including Cook et al., utilize linoleic acid as controls. Clearly, if humans were able to convert linoleic acid into conjugated linoleic acid in any appreciable amount there would be no need for the claimed invention of Cook et al. which is administration of conjugated linoleic acid to a human for the purpose of reducing body fat. One could just administer linoleic acid.

**7. Taken together, these facts rebut any prima facie case of obviousness established by the Office**

As demonstrated above, to the extent that any *prima facie* case of obviousness was established by the Office, it was rebutted by the factual evidence presented during prosecution. At page 12 of the Examiner's Answer, the Examiner alleges that he has established the following:

- Conjugated linoleic acid is taught to reduce body weight;
- bodyweight reduction is correlated with decrease in blood pressure in overweight hypertensive patients;
- linoleic acid is used to treat hypertension; and
- there is no teaching at the time of the invention which would suggest to one of ordinary skill in the art that conjugated linoleic acid would increase blood pressure.

With respect to the first bullet point, Appellants establish above in Section 2 that Cook et al. does not teach that conjugated linoleic acid reduces bodyweight. Cook et al. teaches that conjugated linoleic acid does reduce body fat, but bodyweight is not changed.

With respect to the second bullet point, Appellants first note that this assertion is only relevant if the first bullet point is correct. Because Cook does not teach that conjugated linoleic acid decreases bodyweight, this finding does not support the Examiner's position. Second, the alleged correlation made by the Examiner is irrelevant when a biologically active agent is used. Appellants establish above in Section 5 that when a biologically active agent is used to reduce bodyweight, the biologically active may increase or decrease hypertension. In summary, the effect of the biologically active agent on hypertension is unpredictable. The Examiner takes the position that any decrease in bodyweight will cause a decrease in hypertension. This assertion is rebutted by the evidence submitted by Appellants.

With respect to the third bullet point, Appellants submitted evidence that establishes that when the Shinitzky reference is considered as a whole by a person of skill in the art, the reference teaches that only a complex lipid fraction can be used to treat hypertension. As

discussed above in Section 3, there is no teaching that linoleic acid alone is useful or effective for treating hypertension. Moreover, as established in Section 4 above, Appellants submitted evidence that conjugated linoleic acid has different properties than linoleic acid. As a result, a person of skill in the art would not expect conjugated linoleic acid to have the same properties as linoleic acid for any use, much less for the treatment of hypertension.

With respect to the fourth bullet point, Appellants respectfully submit that the Examiner has not responded to Appellants evidence regarding use of biologically active agents. Appellants have not contended that there is evidence at the time of filing that shows that conjugated linoleic acid would increase blood pressure. Rather, Appellants establish above that when a biologically active agent is given to a subject, the effect of that biologically active agent is unpredictable and that just because an agent can cause a reduction in bodyweight (which is not supported by Cook et al. as discussed above), there is no predictive value to a person of skill in the art that that agent will also decrease blood pressure.

In sum, to the extent that a *prima facie* case of obviousness was presented by the Office, Appellants have presented factual evidence that rebuts the Office's arguments in the form of the Saebo and Bruheim Declarations. Many of the facts in these Declarations were not even addressed by the Office and the Office's arguments regarding the remaining facts are scientifically incorrect and insufficient to rebut the facts contained in the Declarations. Appellants request that the Office find that the rejection is improper.

### **CONCLUSION**

For the foregoing reasons, Appellants respectfully submit that the Examiner's rejection of Claims 1-3, 7 and 9 is erroneous. Reversal of the rejections is respectfully requested. Appellants request that the Board render a decision as to the allowability of the Claims.

Respectfully submitted,

Dated: March 23, 2009

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